

BRIEF COMMUNICATION

Sunlight and Risk of Uveal Melanoma

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Previously, we have presented evidence that exposure to sunlight increases the risk of uveal melanoma (1), as it does for cutaneous melanoma. Despite similar findings from subsequent case-control studies (2-4), this conclusion remains controversial. The hypothesis is, however, supported by the reciprocal threefold increase of eye cancer (predominantly melanoma) following cutaneous melanoma and of cutaneous melanoma following eye cancers (5). Additional corroborating evidence of a role for UV light in uveal melanoma is the occurrence of uveal-tract melanoma at an early age in a Japanese patient with xeroderma pigmentosum (6). Another persistent question regarding the etiology of uveal melanoma is whether ocular nevi or freckles are precursor lesions or markers of increased risk of uveal melanoma (7-9). We now present additional information on sun-related factors from our case-control study of patients with uveal melanoma.

Study subjects were patients referred for the evaluation of uveal melanoma (n = 499), uveal nevi (n = 148), or lesions suspicious for melanoma that were not melanoma or a nevus (pseudomelanomas) (n = 333). All study subjects were examined by one investigator (J. A. Shields). At the time of clinical evaluation, examination data were recorded systematically and included the location of each index lesion (melanoma, nevus, or pseudomelanoma), the

Table 1. Patients with uveal melanoma, uveal nevi, and non-nevus pseudomelanomas of the eye, according to location*

Location	No. with melanoma (%)	No. with nevus (%)	No. with pseudomelanoma (%)
Choroid			
Anterior only	43 (10)†	2 (2)†	14 (6)†
Superior half only	13 (30)	1 (50)	3 (21)
Inferior half only	15 (35)	1 (50)	8 (57)
Both halves	15 (35)		3 (21)
Nasal half only	14 (33)	2 (100)	2 (14)
Temporal half only	10 (23)		4 (29)
Both halves	19 (44)		8 (57)
Posterior only	245 (59)†	118 (98)†	210 (86)†
One area involved			
Central (macula)	28 (11)	16 (14)	40 (19)
Superior nasal	9 (4)	13 (11)	15 (7)
Superior temporal	5 (2)	9 (8)	11 (5)
Inferior nasal	13 (5)	19 (16)	10 (5)
Inferior temporal	7 (3)	18 (15)	24 (11)
Two to three areas involved			
Central + others	151 (62)	27 (23)	58 (28)
Superior without central	4 (2)	2 (2)	2 (1)
Inferior without central	5 (2)	3 (3)	4 (2)
Nasal without central	8 (3)	6 (5)	6 (3)
Temporal without central	9 (4)	4 (3)	7 (3)
More than three areas involved	6 (2)	1 (1)	33 (16)
Anterior and posterior	126 (30)†	0	20 (8)†
Superior half only	23 (18)		1 (5)
Inferior half only	29 (23)		7 (35)
Both halves	74 (59)		12 (60)
Nasal half only	33 (26)		1 (5)
Temporal half only	37 (29)		2 (10)
Both halves	56 (44)		17 (85)
Iris			
Superior half only	0	1 (4)	13 (22)
Inferior half only	14 (78)	20 (80)	28 (48)
Both halves	4 (22)	4 (16)	17 (29)
Nasal half only	2 (11)	0	1 (2)
Temporal half only	10 (56)	14 (76)	37 (80)
Both halves	6 (33)	3 (24)	8 (18)
Ciliary body			
Superior half only	6 (30)	0	0
Inferior half only	6 (30)	0	4 (80)
Both halves	8 (40)	0	1 (20)
Nasal half only	4 (20)	0	1 (20)
Temporal half only	6 (30)	0	3 (60)
Both halves	10 (50)	0	1 (20)

*Location was missing for 47 melanomas (9.4%), three nevi (2.0%), and 26 pseudomelanomas (7.8%).

†Percentages refer to total choroid; subsequent percentages refer to subgroups.

presence and location of additional uveal-tract nevi, and the presence of iris freckles. The most frequent diagnoses for the pseudomelanomas were iridociliary cyst (n = 43), congenital hypertrophy of retinal pigmented epithelium (n = 43), subretinal hemorrhage (n = 22), and choroidal hemangioma (n = 20). For choroidal lesions, the superior/inferior, anterior/posterior, and tem-

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See "Note" section following "References."

Table 2. Number of patients and estimated RR of uveal melanoma and nevi in the iris and in the choroid or ciliary body, according to presence of ocular pigmented lesions and skin freckles

	Non-nevus pseudomelanoma	Iris		Choroid/ciliary body	
		Uveal melanoma	Nevus	Uveal melanoma	Nevus
Iris freckles					
None	309	29	20	422	109
Some	21	5	7	37	11
RR*	1.0	2.5	5.0	1.3	1.5
95% CI		0.9-7.2	1.9-13	0.7-2.3	0.7-3.3
Iris nevi					
None	308	27	8	420	104
Some	22	7	12	39	16
RR*	1.0	3.6	33	1.3	2.1
95% CI		1.4-9.2	13-84	0.7-2.2	1.0-4.2
	Non-nevus pseudomelanoma	Uveal melanoma of the iris		Uveal melanoma of the choroid/ciliary body	
		No.	RR (95% CI)	No.	RR (95% CI)
Iris and skin freckles					
No iris, <25 skin	184	15	1.0	239	1.0
No iris, ≥25 skin	68	12	2.2 (1.0-4.8)	128	1.4 (1.0-2.1)
Some iris, <25 skin	15	2	1.6 (0.4-7.1)	22	1.1 (0.6-2.2)
Some iris, ≥25 skin	4	2	6.1 (1.2-32)	13	2.5 (0.8-7.4)

*RRs are derived from separate polychotomous logistic regression models with adjustment for sex and age.

poral/nasal positions were noted; for the iris and ciliary body lesions, the superior/inferior and temporal/nasal positions were recorded. Estimates of relative risk (RR)—the ratio of risk in an exposed group to risk in an unexposed group—were adjusted for potentially confounding factors by stratification techniques (10) and by logistic regression for polychotomous outcomes (11), a method that accounts for using a single control group with four case groups in its estimation of variance. Information on skin freckles was obtained from interview data.

The index lesions, melanomas, nevi, and pseudomelanomas, were not evenly distributed in the uveal tract (Table 1). Among the choroidal lesions, all were more common in the posterior choroid. In the anterior choroid, the lesions were evenly distributed. In the posterior choroid, the melanomas preferentially involved the central area (73%). The nevi and pseudomelanomas involved the central area to a lesser extent (37% and 47%, respectively). The iris lesions were more common in the inferior and temporal areas. The ciliary body lesions, similar to those in the anterior choroid, were evenly distributed. The choroidal

and iris melanomas were thus located most frequently in the areas that presumably are exposed to the most sunlight. The distribution of lesions in the lateral and inferior portion of the iris was most striking for the melanomas, and the benign nevi and was somewhat attenuated in the pseudomelanomas.

Iris freckles and additional nevi were seen more commonly among patients diagnosed with iris melanoma or nevi than among those with a choroidal/ciliary body lesion or with pseudomelanoma (Table 2). Our data suggest iris freckles and nevi may be risk factors for uveal melanoma. This finding would be expected if iris freckles are a marker of sunlight exposure, as are cutaneous freckles. Similar risks for the nevi are consistent with the relationship of uveal nevi to sun exposure. Table 2 also shows that patients with iris freckles and 25 or more cutaneous freckles had the greatest RR of uveal melanoma, especially of the iris. The finding of a greater effect in the iris is consistent with sun exposure, since the lens filters much of the UV radiation after childhood.

Although the biologic explanation of the association of sunlight exposure and uveal melanoma is not completely clear,

there are data now from three studies, including this one, that people who develop uveal melanoma report having increased sun exposure (2,3). These additional clinical data corroborate the interview data. The striking preponderance of melanomas in the central posterior and sunlit inferior and temporal portions of the iris offers a compelling argument that sunlight induces uveal as well as cutaneous melanoma. The similar risks for uveal nevi suggest that they may also be sunlight related. The role of sun exposure in the etiology of uveal melanoma is supported also by the distribution of iris freckles and cutaneous freckles among our patients and by indirect evidence from the literature on second cancer and xeroderma pigmentosum (5,6). If these observations are correct, the etiology of uveal melanoma may be more similar to cutaneous melanoma than previously thought and similar precautions against sun exposure may be warranted for populations at greatest risk.

References

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Note

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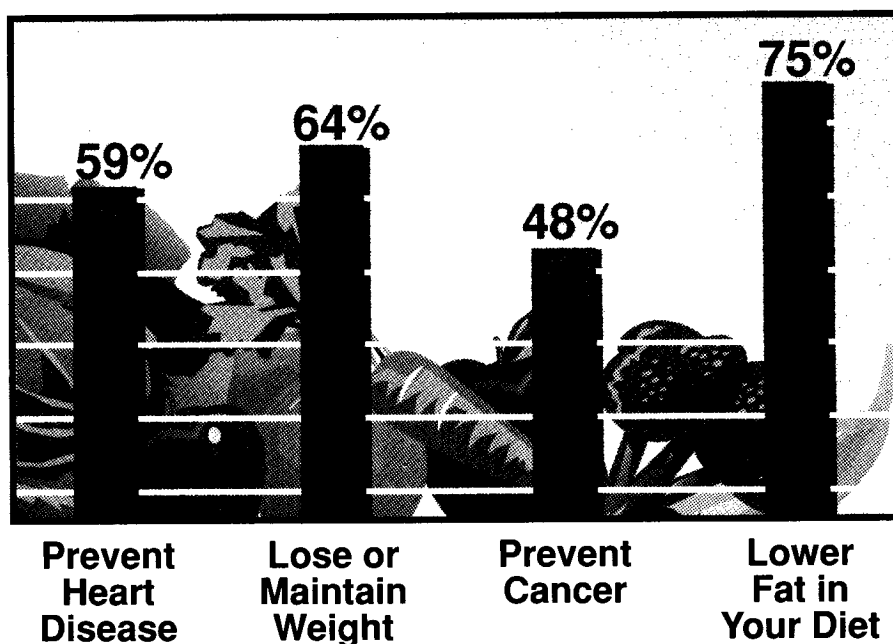
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Why eat five?

As the link between diet and overall health continues to gain attention, public awareness of the benefits of fruits and vegetables has expanded. In a recent survey, 1,003 people were asked how likely they thought it is that eating fruits and vegetables can help reduce the risk of several health conditions.

Perceived health benefits most frequently mentioned were:



JOHN SHERLOCK

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